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DOI: https://doi.org/10.3987/COM-06-S(K)47

FORMATION OF PHOSPHONYLATED THIIRANES IN THE REACTION OF A DIAZOMETHANEPHOSPHONATE AND CYCLOALIPHATIC THIOKETONES

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Dedicated to Professor Yoshito Kishi at the occasion of his 70th birthday

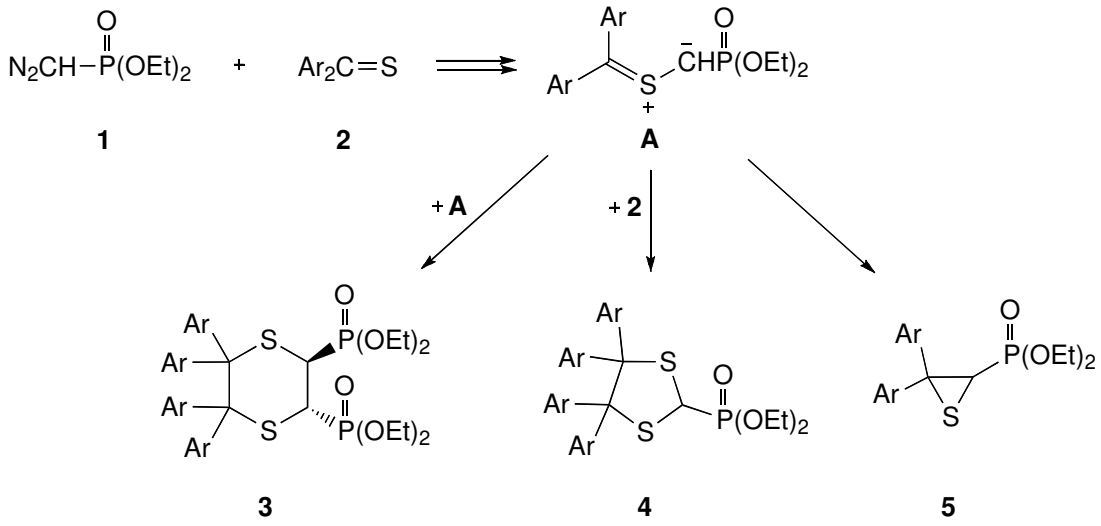
Abstract – The reaction of diethyl diazomethanephosphonate (**1**) with cycloaliphatic thioketones (**6**) in THF at room temperature leads to the corresponding thiirane-2-phosphonates (**7**) in good yield. A reaction mechanism via 1,3-dipolar cycloaddition of the diazo compound with the C=S group to give the 2,5-dihydro-1,3,4-thiadiazole-2-phosphonate as an intermediate, which spontaneously eliminates nitrogen is most likely. The resulting thiocarbonyl ylide undergoes a 1,3-dipolar electrocyclization to yield a thiirane. These products can be desulfurized smoothly by treatment with tris(diethylamino)phosphine to give α,β-unsaturated phosphonates.

INTRODUCTION

In a recent paper we described the reaction of diethyl diazomethanephosphonate (**1**) with aromatic thioketones (**2**).[1] The most reactive thioketones, i.e., 9*H*-fluorene-9-thione and thiobenzophenone, in THF reacted with **1** at temperatures below 0 °C to give 1,4-dithianes (**3**) and 1,3-dithiolanes (**4**), respectively (*Scheme 1*). On the other hand, the less reactive 9*H*-xanthene-9-thione and **1** in refluxing toluene yielded the corresponding thiirane (**5**) together with the phosphonylated ethylene as the product of a spontaneous

desulfurization. The formation of all these products can be explained by subsequent reactions of in situ generated thiocarbonyl ylides of type **A**. These sulfur-containing 1,3-dipoles have been studied extensively in recent time.[2,3] It is well established that the reaction of thiocarbonyl compounds with diazo compounds offers a very efficient access to these reactive intermediates, which are attractive building blocks for the preparation of diverse thiaheterocycles.[4] The use of phosphonylated diazomethanes opens a convenient route to phosphonylated products in a one-pot reaction.

Scheme 1



Thiiranes are useful three-membered heterocycles which can be applied in the synthesis of more complex systems.[5] Furthermore, some thiiranes found application as pharmaceuticals, agrochemicals or materials with special properties.[6] It is also well known that the phosphonyl group is an important unit in organic compounds with respect to their biological activities and physicochemical properties.[7] For this reason, hitherto very little known phosphonylated thiiranes of type (**5**) attracted our interest. The earlier studies (see ref.[3]) showed that aliphatic thiocarbonyl ylides prefer to undergo a 1,3-dipolar electrocyclization to give thiiranes instead of dimerization to **3** and 1,3-dipolar cycloadditions to yield **4**.

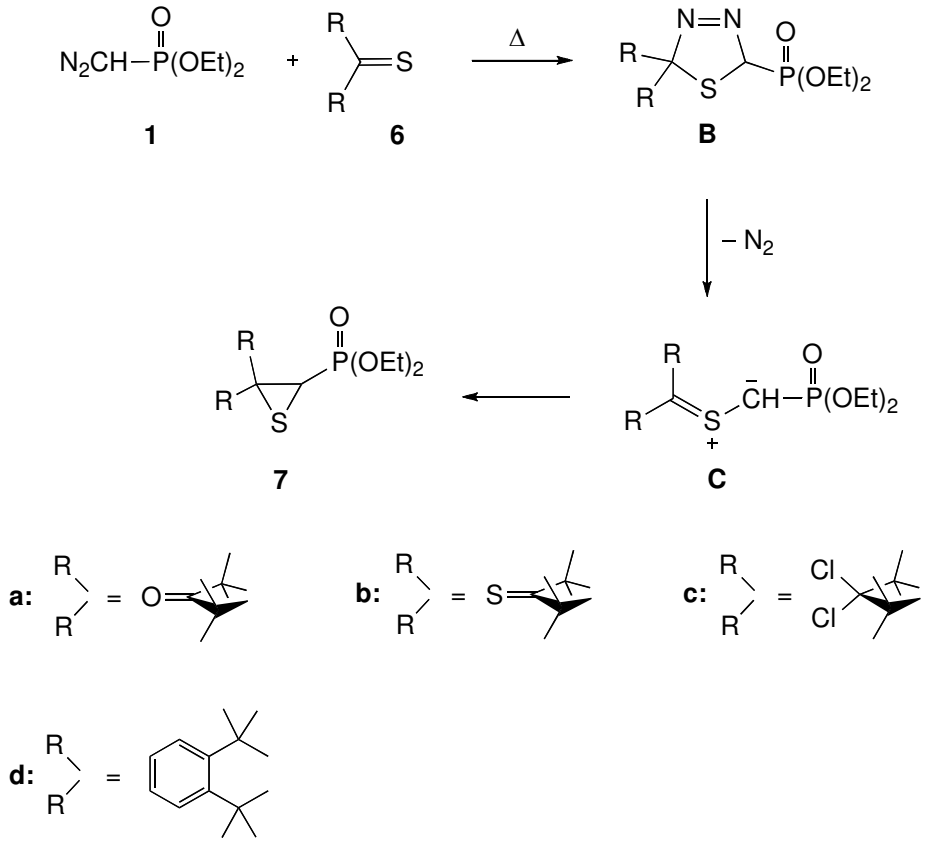
The aim of the present work was to examine the behavior of **1** in reactions with a series of cycloaliphatic thioketones (**6**) and to compare the reactivity of **1** with that of ethyl diazoaceate, which was the subject of an earlier study.[8]

RESULTS AND DISCUSSION

The sterically crowded 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**6a**)[9] and the corresponding dithione (**6b**)[10] are favorite model compounds for studies on the reactivity of the C=S function. Recently, we described the synthesis of 3,3-dichloro-2,2,4,4-tetramethylcyclobutanethione (**6c**) as a new example of a

stable and synthetically useful thioketone.[11,12] Typically, equimolar amounts of **1** and **6** in THF solution were heated to reflux whereby evolution of N_2 was observed. After 1–5 h, the red color of **6** vanished indicating the completion of the reaction. The ^{1}H-NMR spectrum of the crude mixtures showed in each case the formation of only one product in almost quantitative yield, which are characterized by a doublet at ca. 2.70–3.05 ppm with $^2J_{H,P} \approx 9.4$ Hz. Pure products were obtained in moderate yields after crystallization from hexane. Attempted chromatographic workup led to decomposition of the products. The crystalline compounds were identified as thiiranes (**7a**–**c**) on the basis of their spectroscopic and analytical data (*Scheme 2*). In the reaction of **1** with 1,1,3,3-tetramethylindane-2-thione (**6d**) in THF under reflux, the expected thiirane (**7d**) was obtained as the sole product.

Scheme 2

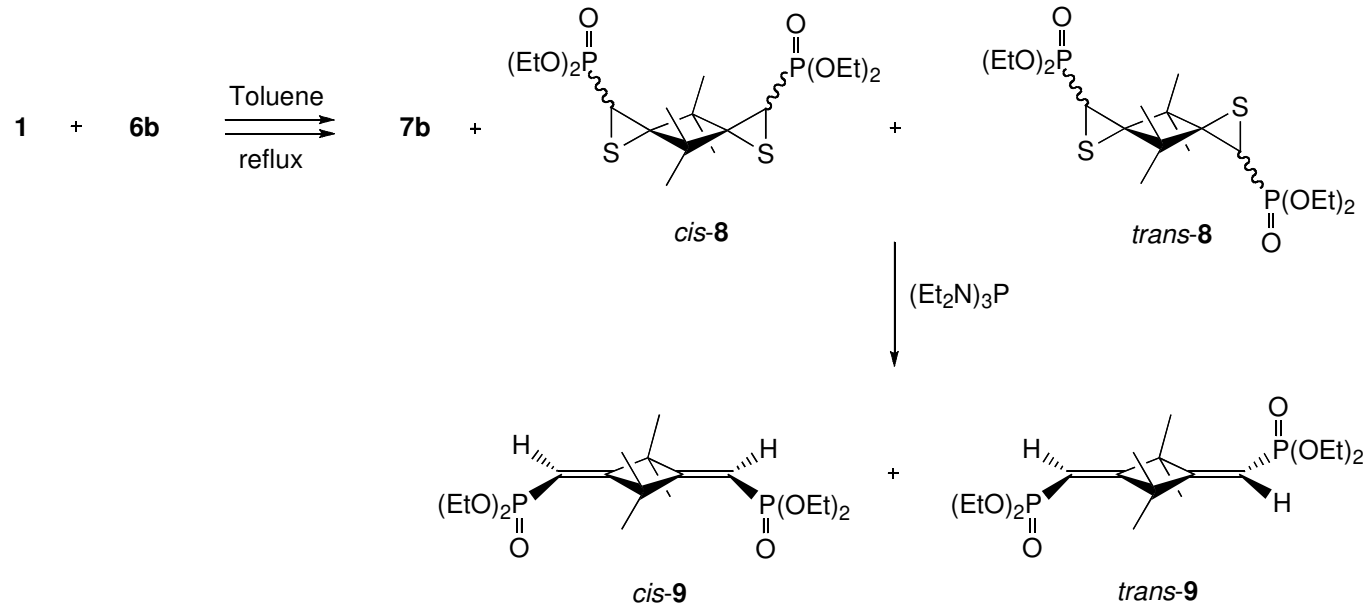


In order to test the thermal stability of the thiiranes (**7**), the reaction of **1** with **6a** was carried out in refluxing toluene. After addition of **6a**, the decolorization occurred immediately. According to the ^{1}H-NMR spectrum, **7a** was formed quantitatively, and no desulfurized product could be detected.

The analogous reaction of equimolar amounts of **1** and **6b** in refluxing toluene gave a mixture of **7b** and the stereoisomeric 2:1 products (*cis*-**8**) and (*trans*-**8**) (*Scheme 3*). When **1** was used in a three-fold excess, the mixture contained only bisthiiranes **8** as a mixture of four diastereoisomers, which could be separated

neither by fractional crystallization nor by column chromatography. Desulfurization of the mixture obtained after attempted crystallization from hexane yielded the two bis-phosphonates *cis*-**9** and *trans*-**9** in a ratio of 1:4 (^{1}H-NMR). After crystallization and subsequent separation by preparative layer chromatography, the *trans*-isomer was obtained in pure form, which showed only one signal for 4 Me groups at 1.49 and 25.9 ppm, respectively.[13]

Scheme 3

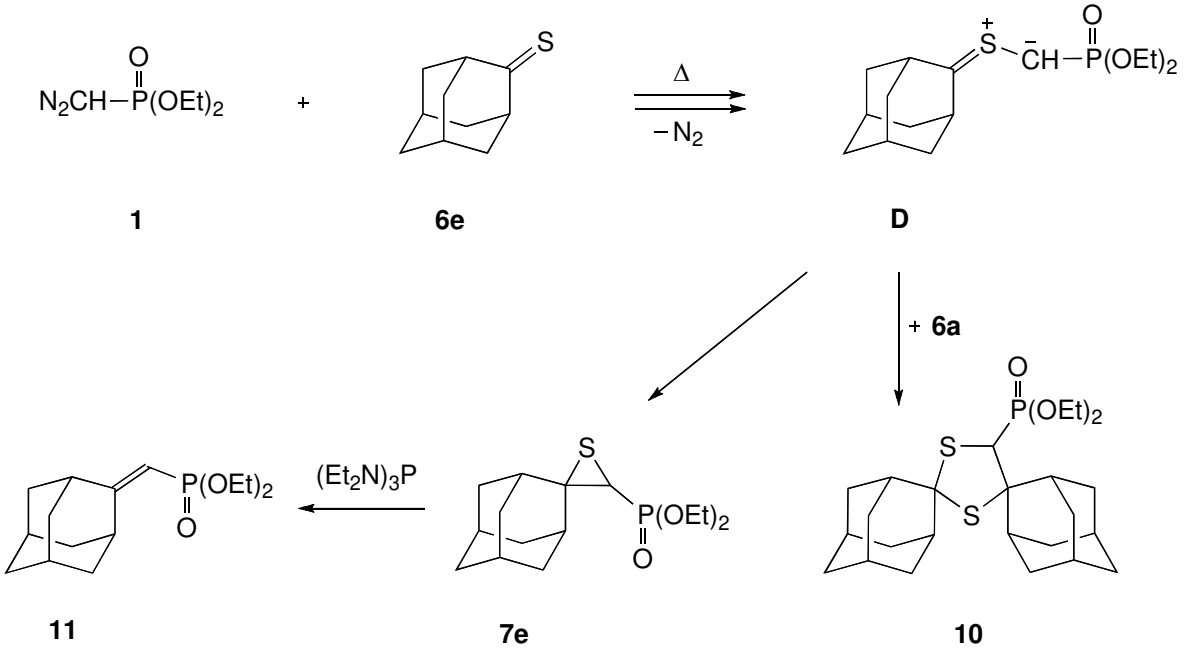


Whereas the reaction of **1** with adamantanethione (**6e**) in boiling toluene afforded the phosphonylated thiirane (**7e**) exclusively, heating of a mixture of **1** and **6e** in THF led to **7e** along with a second product, which in the ^{1}H-NMR spectrum showed a doublet located at 2.9 ppm ($^2J_{H,P} \approx 15.2$ Hz). After decolorization of the reaction mixture, the ^{1}H-NMR spectrum evidenced the presence of substantial amounts of **1**, which only after addition of another 0.5 equivalents of **6e** was completely consumed. In analogy to the thiiranes (**7a**–**d**), the doublet at 2.65 ppm ($^2J_{H,P} \approx 9.6$ Hz) can be attributed to **7e**. For the second product, the structure of 1,3-dithiolane (**10**) is likely, similar to the result of the reaction of **6e** with ethyl diazoacetate.[8] All attempts to separate **7e** and **10** by chromatography (SiO_2) or crystallization were unsuccessful. For this reason, the crude reaction mixture, which was obtained in boiling toluene, was desulfurized by heating it with $(Et_2N)_3P$ in THF solution. After chromatographic workup, (adamantylidene)methanephosphonate (**11**, *Scheme 4*) was isolated as a viscous oil in 56% yield.

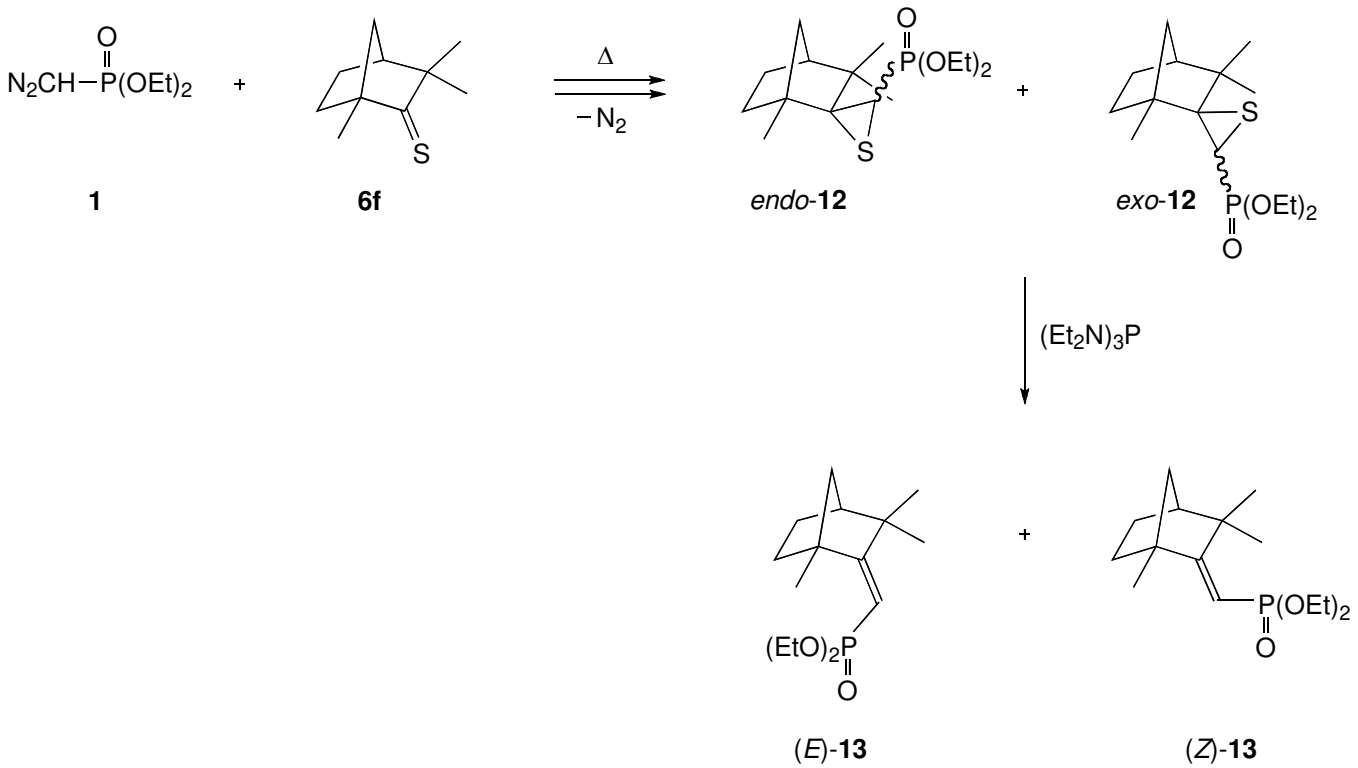
For the reaction of **1** with thiofenchone (**6f**), four stereoisomeric thiiranes can be expected.[14] However, the experiment carried out in refluxing toluene gave only two products, which were identified by ^{1}H-NMR spectroscopy as thiiranes of type (**12**), based on the presence of two doublets at 2.75 and 2.80 ppm with $^2J_{H,P} \approx 4.8$ Hz and 3.6 Hz, respectively. The ratio of the products was estimated to *ca.* 3:1.[16] Similar

to the examples shown in *Scheme 3* and *4*, desulfurization occurred smoothly by treatment with $(Et_2N)_3P$, leading to a mixture of (*E*)-and (*Z*)-**13**, in which the ratio of the components is preserved (*Scheme 5*). After column chromatography (SiO_2), the major isomer was isolated in pure form.

Scheme 4

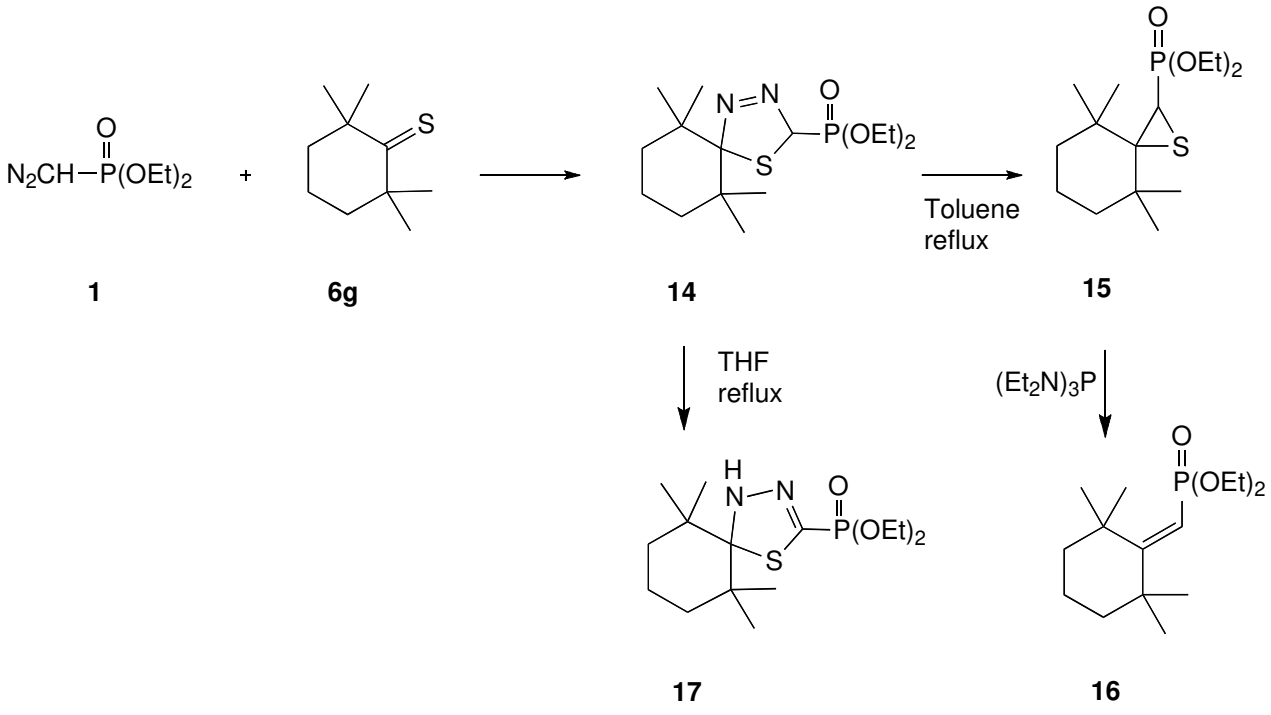


Scheme 5



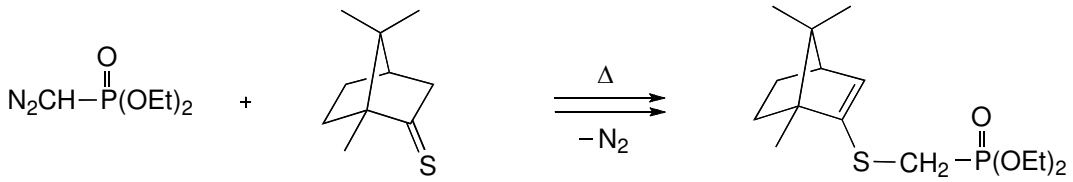
The sterically crowded 2,2,6,6-tetramethylcyclohexanethione (**6g**) reacted with **1** in boiling toluene to give thiirane (**15**), which without isolation was desulfurized by treatment with $(Et_2N)_3P$ to give the expected α,β-unsaturated phosphonate (**16**) in 53% yield (*Scheme 6*). However, in a single experiment, which was carried out in refluxing THF solution, no evolution of N_2 was observed, indicating that no thiocarbonyl ylide is formed. In contrast to other products of the reactions of **1** and **6a–f**, the ^{1}H-NMR spectrum of the crystalline material obtained from **1** and **6g** in this experiment did not reveal any signal around 2.5 ppm, which is characteristic for CH of thiiranes of type **7**. Instead, a broad signal appeared at 6.60 ppm. In the IR spectrum (KBr), an absorption at 3250 cm^{-1} indicated the presence of an NH group. The MS spectrum and the elemental analyses confirmed the molecular formula of 1:1 adduct of **1** and **6g**. Based on these data and in analogy to a previously described compound,[17] the structure of the 2,3-dihydro-1,3,4-thiadiazole (**17)** was attributed to this product (*Scheme 7*). A fast tautomerization of the initially formed **14** offers a plausible explanation for the formation of **17**.[18]

Scheme 6



Thiocamphor (**6h**) is known to undergo easily [2+3]-cycloadditions with diazomethane below 0 °C.[15] Subsequent elimination of N_2 at 10 °C leads to 2-methylsulfanyl-2-bornene, which is an isomer of the intermediate thiocarbonyl *S*-methanide. The formation of this product is explained by a 1,4-H-shift in the ylide (see also ref.[20]). In the present study, heating of a mixture of **1** and **6h** in THF yielded again only one product (^{1}H-NMR) with two doublets at 2.94 ($^2J_{H,P} \approx 16.0$ Hz) and 5.58 ppm ($^3J_{H,H} \approx 4.3$ Hz). These data are in accordance with structure (**18**, *Scheme 7*), which is formed *via* an analogous 1,4-H-shift.

Scheme 7



1 **6h** **18**

In conclusion, reactions with aliphatic thioketones extend the synthetic applications of diazomethane phosphonates and open a straightforward access to phosphonylated thiiranes (**7**). These products can be desulfurizated smoothly to give α,β-unsaturated phosphonates. From the mechanistic point of view, the reactions proceed *via* a regioselective [2+3]-cycloaddition, followed by N_2 elimination leading to reactive thiocarbonyl ylides, which, on turn, undergo a 1,3-dipolar electrocyclization. In contrast, the more reactive aromatic thioketones and **1** form phosphonylated thiocarbonyl ylides, which preferably dimerize or capture the starting thioketone to give 1,3-dithiolanes (*Schönberg* products).[1]

EXPERIMENTAL

General remarks. Melting points were determined in a capillary using a *MEL-TEMP II* apparatus (*Aldrich*) and are uncorrected. IR spectra were recorded in KBr pellets or as films with a *Nexus* spectrophotometer. ^{1}H-NMR, ^{13}C-NMR, and ^{31}P-NMR spectra were registered in $CDCl_3$ on a *Tesla BS 687* instrument (^{1}H at 80 MHz) or a *Bruker AC-300* spectrometer (^{1}H at 300, ^{13}C at 75, and ^{31}P at 121 MHz, resp.) using TMS (δ = 0 ppm) as an internal and 85% H_3PO_4 as an external standard. ^{13}C-NMR peak assignments were made on the basis of DEPT measurements. MS (CI) were recorded on a *Finnigan-Mat-90* or *Finnigan-SSQ-700* spectrometer; *m/z* (rel.%). Elemental analyses were performed in the Analytical Laboratory of the University of Zürich.

Starting materials. Ethyl diazomethanephosphonate (**1**) was prepared by the *Seyferth* method.[21] 2,2,4,4-Tetramethyl-3-thioxocyclobutanone (**6a**),[22] 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**6b**),[22] 3,3-dichloro-2,2,4,4-tetramethylcyclobutanethione (**6c**),[11] 2-adamantanethione (**6e**),[23] 1,1,3,3-tetramethylindan-2-thione (**6d**),[24] 2,2,6,6-tetramethylcyclohexanethione (**6g**),[25] thiofenchone (**6f**),[26] and thiocamphor (**6h**)[26] were synthesized by thionation of corresponding ketones following the literature procedure.

Reactions of thioketones **6a–d** *with diethyl diazomethanephosphonate* (**1**)*; isolation of thiiranes* **7a–d**. *General procedure***.** A solution of the corresponding thione **6** (1 mmol) and **1** (1 mmol) in dry THF (1

mL) was heated under reflux for 1 h (5 h in the case of **6d**). After evaporation of the solvent, the crude mixtures were analyzed by ^{1}H-NMR spectroscopy and purified by crystallization. Yields refer to isolated and purified products.

Diethyl (4,4,6,6-tetramethyl-5-oxo-1-thiaspiro[2.3]hexane)-2-phosphonate (**7a**). Yield: 180 mg (59%). Colorless crystals (hexane); mp 71–73 °C. IR (KBr): 2958*s*, 2929*m*, 1783*vs* (C=O), 1460*m*, 1442*m*, 1256*s* and 1242*s* (P=O), 1047*vs* and 1022*vs* (P–O–C), 971*s*, 540*s*. ^{1}H-NMR ($CDCl_3$): 1.09 (*d*, $J_{H,P}$ = 1.3 Hz, Me), 1.27, 1.31, 1.53 (3*s*, 3 Me), 1.36, 1.37 (2*t*, $J_{H,H}$ = 7.1 Hz, 2 *Me*CH_2O), 2.99 (*d*, $^{2}J_{H,P}$ = 9.4 Hz, CH), 4.15–4.27 (*m*, 2 MeC*H*$_2$O). ^{13}C-NMR ($CDCl_3$): 16.4, 16.5 (2*d*, $^{3}J_{C,P} \approx$ 6.7 Hz, 2 *Me*CH_2O), 22.5, 22.7, 23.4, 24.0 (4 Me), 31.5 (*d*, $^{1}J_{C,P}$ = 192 Hz, CH), 61.9, 62.3 (2*s*, 2 C_q), 63.2, 63.4 (2*d*, $^{2}J_{C,P} \approx$ 6.8 Hz, 2 Me*C*H_2O), 65.7 (*d*, $^{2}J_{C,P}$ = 2.8 Hz, C_qS), 218.5 (C=O). ^{31}P-NMR ($CDCl_3$): 20.97. CI-MS (NH_3): 630 (6, $[2M+NH_4]^+$), 613 (19, $[2M+1]^+$), 581 (11), 325 (16), 324 (100, $[M+NH_4]^+$), 307 (31). Anal. Calcd for $C_{13}H_{23}O_4PS$: C, 50.97; H, 7.57; S, 10.47. Found: C, 50.63; H, 7.63; S, 10.15.

Diethyl (4,4,6,6-tetramethyl-5-thioxo-1-thiaspiro[2.3]hexane)-2-phosphonate (**7b**). Yield: 200 mg (62%). Orange crystals (petroleum ether); mp 82–84 °C. IR (KBr): 2971*s*, 2953*s*, 1451*m*, 1394*m*, 1299*s*, 1239*vs* (P=O), 1107*s*, 1048*vs* and 1019*vs* (P–O–C), 975*s*, 870*m*, 541*m*. ^{1}H-NMR ($CDCl_3$): 1.16, 1.33, 1.36, 1.60 (4*s*, 4 Me), 1.37–1.40 (*m*, 2 *Me*CH_2O), 3.03 (*d*, $^{2}J_{H,P}$ = 9.2 Hz, CH), 4.16–4.27 (*m*, 2 MeC*H*$_2$O). ^{13}C-NMR ($CDCl_3$): 16.4, 16.5 (2*d*, $^{3}J_{C,P} \approx$ 6.7 Hz, 2 *Me*CH_2O), 26.3, 26.5, 27.4, 28.1 (4 Me), 32.1 (*d*, $^{1}J_{C,P}$ = 191 Hz, CH), 63.2, 63.4 (2*d*, $^{2}J_{C,P} \approx$ 6.9 Hz, 2 Me*C*H_2O), 64.3, 65.5 (2*s*, 2 C_q), 69.2 (*d*, $^{2}J_{C,P}$ = 3.0 Hz, C_qS), 275.9 (C=S). ^{31}P-NMR ($CDCl_3$): 21.45. CI-MS (NH_3): 340 (8, $[M+NH_4]^+$), 325 (10), 323 (100, $[M+1]^+$), 291 (5). Anal. Calcd for $C_{13}H_{23}O_3PS_2$: C, 48.43: H, 7.19; S, 19.89. Found: C, 48.34; H, 7.16; S, 19.59.

Diethyl (5,5-dichloro-4,4,6,6-tetramethyl-1-thiaspiro[2.3]hexane)-2-phosphonate (**7c**). Yield: 220 mg (61%). Colorless crystals (hexane); mp 48–50 °C. IR: 2988*s*, 2931*m*, 1466*m*, 1370*m*, 1259*s* and 1244*s* (P=O), 1054*vs* and 1030*vs* (P–O–C), 973*s*, 920*s*, 817*m*, 533*m*. ^{1}H-NMR ($CDCl_3$): 1.13, 1.35, 1.48, 1.69 (4*s*, 4 Me), 1.36-1.38 (*m*, 2 *Me*CH_2O), 2.67 (*d*, $^{2}J_{H,P}$ = 8.2 Hz, CH), 4.14–4.23 (*m*, 2 MeC*H*$_2$O). ^{13}C-NMR ($CDCl_3$): 16.4, 16.5 (2*d*, $^{3}J_{C,P} \approx$ 6.0 Hz, 2 *Me*CH_2O), 26.0, 26.3, 26.9, 27.8 (4 Me), 29.8 (*d*, $^{1}J_{C,P}$ = 192 Hz, CH), 54.2 (*s*, C_q), 55.3 (*d*, $^{3}J_{C,P}$ = 2.4 Hz, C_q), 63.0, 63.4 (*d*, $^{2}J_{C,P} \approx$ 6.8 Hz, Me*C*H_2O), 67.1 (*d*, $J_{C,P}$ = 3.0 Hz, C_qS), 100.0 (*s*, CCl_2). ^{31}P-NMR ($CDCl_3$): 21.01. CI-MS (NH_3): 691 (8), 378 (100, $[M+NH_3]^+$), 346 (34), 329 (30), 291 (5). Anal Calcd for $C_{13}H_{23}O_3Cl_2PS$: C, 43.22; H, 6.42; S, 8.57. Found: C, 43.17; H, 6.31; S, 8.46.

Diethyl (1,1,3,3-tetramethylindane-2-spiro-2´-thiirane)-3-phosphonate (**7d**). Yield: 230 mg (65%). Colorless crystals (hexane); mp 80–83 °C. IR: 2975*s*, 2931*m*, 1632*m*, 1483*s*, 1257*s* (P=O), 1052*vs* and

1025*vs* (P–O–C), 973*s*, 766*s*, 756*s*, 540*m*, 526*m*. ^{1}H-NMR ($CDCl_3$): 1.13, 1.43, 1.53, 1.64 (4*s*, 4 Me), 1.34–1.42 (*m*, 2 *Me*CH_2O), 2.76 (*d*, $^2J_{H,P}$ = 5.0 Hz, CH), 4.17–4.31 (*m*, 2 MeC*H*$_2$O), 7.13–7.29 (*m*, 4 arom. H). ^{13}C-NMR ($CDCl_3$): 16.4, 16.6 (2*d*, $^3J_{C,P} \approx$ 5.9 Hz, 2 *Me*CH_2O), 27.2, 30.3, 30.9, 32.6 (4 Me), 30.7 (*d*, $^1J_{C,P}$ = 194 Hz, CH), 47.0 (*d*, $^3J_{C,P}$ = 2.0 Hz, C_q), 48.4 (*s*, C_q), 62.4, 63.4 (2*d*, $J_{C,P} \approx$ 6.8 Hz, 2 Me*C*H_2O), 73.9 (*d*, $^2J_{C,P}$ = 3.0 Hz, C_qS), 122.0, 122.4, 127.2, 127.6 (4 arom. CH), 147.3, 150.2 (2 arom. C_q). CI-MS (NH_3): 645 (8), 372 (30, $[M+NH_4]^+$), 340 (24), 323 (100). Anal. Calcd for $C_{18}H_{27}O_3PS$: C, 60.99; H, 7.68; S, 9.05. Found: C, 60.65; H, 7.66; S, 9.00.

Reactions of thioketones **6b, 6e**–**6g** *with diethyl diazomethylphosphonate* (**1**); *desulfurization of thiiranes* **7e, 8, 12** *and* **15** *with tris(diethylamino)phosphine. General procedure*. To a boiling solution of **1** (1 mmol, in the case of **6b**, 3 mmol of **1** were used) in toluene (2–5 mL) was portionally added **6b** or **6e** (1 mmol) in toluene (5–10 mL). The mixtures were heated under reflux for 2–3 h. Thiones **6f** and **6g** and **1** were heated in dry THF (2 mL) for 0.5–2 h. After completion of the reaction and evaporation of the solvent, the crude mixture was crystallized from hexane to give a mixture of thiiranes as a colorless solid. This material was treated with $(Et_2N)_3P$ (1.2 mmol) in refluxing dry THF (2 mL) for 2–4 h yielding a 1:4 mixture of *cis*-**9** and *trans*-**9**. The products were separated chromatographically (SiO_2, hexane/AcOEt: 3.5:1.5). In the case of **6b**, an analytically pure sample was obtained after crystallization from hexane in dry ice. Yields refer to isolated and purified products.

Diethyl ({3-[(diethoxyphosphoryl)methylene]-2,2,4,4-tetramethylcyclobutan-1-ylidene)methanephosphonate (**9**). After layer chromatography, a single isomer of **9**, *i.e.*, *trans*-**9**, was isolated. Yield: 200 mg (51%). Colorless crystals (hexane); mp 80–82 °C. IR: 2983*m*, 2961*m*, 1634*s*, 1249*vs* (P=O), 1050*vs* and 1030*vs* (P–O–C), 964*s*, 855*m*, 823*m*, 553*m*. ^{1}H-NMR ($CDCl_3$): 1.33 (*t*, $J_{H,H}$ = 7.1 Hz, 2 *Me*CH_2O), 1.49 (*s*, 4 Me), 4.06 (*quint*-like, $J_{H,H} \approx J_{H,P} \approx$ 7 Hz, 2 MeC*H*$_2$O), 5.45 (*d*, $J_{H,P}$ = 14.0 Hz, 2 =CH). ^{13}C-NMR ($CDCl_3$): 16.2 (*d*, $^3J_{C,P}$ = 6.4 Hz, 2 *Me*CH_2O), 25.9 (4 Me), 52.1 (*dd*, $^3J_{C,P}$ = 22.4 and 8.7 Hz, 2 C_q), 61.2 (*d*, $^2J_{C,P}$ = 5.4 Hz, 2 Me*C*H_2O), 105.4 (*d*, $^1J_{C,P}$ = 192.2 Hz, =CH), 182.4 (*s*, C_q). ^{31}P-NMR ($CDCl_3$): 16.93. CI-MS (NH_3): 410 (20), 409 (100, $[M+1]^+$). Anal. Calcd for $C_{18}H_{34}O_6P_2$: C, 52.94; H, 8.39. Found: C, 52.47; H, 8.33.

Diethyl (adamantan-2-ylidene)methanephosphonate (**11**). Yield: 160 mg (56%). Colorless, thick oil. IR: 2980*m*, 2907*s*, 2852*m*, 1625*m*, 1450*m*, 1244*s* (P=O), 1055*vs* and 1028*vs* (P–O–C), 961*s*, 819*m*. ^{1}H-NMR ($CDCl_3$): 1.32 (*t*, $J_{H,H}$ = 7.1 Hz, 2 *Me*CH_2O), 1.78–1.90, 1.90–2.02 (2*m*, 12 H), 2.48 (br *s*, 1 H), 3.50 (br *s*, 1 H), 4.06 (*quint*-like, $J_{H,H} \approx J_{H,P} \approx$ 7 Hz, 2 MeC*H*$_2$O), 5.27 (*d*, $J_{H,P}$ = 20.5 Hz, =CH). ^{13}C-NMR ($CDCl_3$): 16.3 (*d*, $^3J_{C,P}$ = 6.6 Hz, 2 *Me*CH_2O), 27.6 (2 CH), 35.2 (*d*, $^3J_{C,P} \approx$ 7 Hz, CH), 36.6, 39.1, 39.8 (4 CH_2),

42.5 (*d*, $^{3}J_{C,P} \approx 25$ Hz, CH), 61.0 (2 Me*C*H_2O), 103.6 (*d*, $^{1}J_{C,P} = 187.9$ Hz, =CH), =C not detected. ^{31}P-NMR ($CDCl_3$): 19.58. CI-MS (NH_3): 286 (17), 285 (100, $[M+1]^+$). Anal. Calcd for $C_{15}H_{25}O_3P$: C, 63.36; H, 8.86. Found: C, 63.43; H, 8.90.

Diethyl (1,3,3-trimethylbicyclo[2.2.1]heptan-2-ylidene)methanephosphonate (**13**). A 4:1 mixture of ismeric compounds **13** (*Z*- and *E*- attribution is unknown) was obtained as the crude product. Yield: 200 mg (70%). After column chromatography (SiO_2), a single isomer of **13** was isolated as yellowish, thick oil. IR (neat): 2977*s*, 2961*s*, 1626*m*, 1240*s* (P=O), 1055*vs* and 1030*vs* (P–O–C), 961*s*, 823*m*. ^{1}H-NMR ($CDCl_3$): 1.05, 1.07, 1.57 (3*s*, 3 Me), 1.25 (*d*-like, 2 H), 1.33 (*t*, $J_{H,H} = 7.1$ Hz, 2 *Me*CH_2O), 1.40–1.95 (*m*, 5 H), 4.00–4.14 (*m*, 2 MeC*H*$_2$O), 5.23 (*d*, $J_{H,P} = 14.0$ Hz, =CH). ^{13}C-NMR ($CDCl_3$): 16.2 (*d*, $^{3}J_{C,P} = 6.7$ Hz, 2 *Me*CH_2O), 19.2, 26.3, 28.6 (3 Me), 25.1, 35.0, 46.0 (3 CH_2), 46.4 (CH), 47.4 (*d*, $^{3}J_{C,P} = 19.3$ Hz, C_q), 52.3 (*s*, C_q), 61.0 (*d*, $^{3}J_{C,P} = 22.3$ Hz, 2 Me*C*H_2O), 102.3 (*d*, $^{1}J_{C,P} = 197.0$ Hz, =CH), =C not detected. ^{31}P-NMR ($CDCl_3$): 20.00. CI-MS (NH_3): 288 (17), 287 (100, $[M+1]^+$), 286 (7).

Diethyl (2,2,6,6-tetramethylcyclohexylidene)methanephosphonate (**16**). Yield: 150 mg (53%). Yellowish, thick oil. IR (neat): 2962*s*, 2932*s*, 2870*m*, 1585*m*, 1467*m*, 1389*m*, 1366*m*, 1243*s* (P=O), 1056*vs* and 1030*vs* (P–O–C), 958*s*, 784*m*, 567*m*. ^{1}H-NMR ($CDCl_3$): 1.18, 1.42 (2*s*, 4 Me), 1.327, 1.328 (2*t*, $J_{H,H} = 7.0$ Hz, 2 *Me*CH_2O), 1.45–1.55 (*m*, 4 H), 1.60–1.68 (*m*, 2 H), 4.00–4.12 (*m*, 2 MeC*H*$_2$O), 5.63 (*d*, $J_{H,P} = 8.1$ Hz, =CH). ^{13}C-NMR ($CDCl_3$): 16.2 (*d*, $^{3}J_{C,P} = 6.6$ Hz, 2 *Me*CH_2O), 17.6 (CH_2), 30.4, 32.4 (2 Me), 37.6 (*s*, C_q), 38.5, 40.9 (2 CH_2), 39.5 (*d*, $^{3}J_{C,P} \approx 7$ Hz, C_q), 61.0 (*d*, $^{3}J_{C,P} = 6.2$ Hz, 2 Me*C*H_2O), 110.0 (*d*, $^{1}J_{C,P} = 192.7$ Hz, =CH), =C not detected. ^{31}P-NMR ($CDCl_3$): 20.36. CI-MS (NH_3): 290 (17), 289 (100, $[M+1]^+$). Anal. Calcd for $C_{15}H_{29}O_3P$: C, 62.48; H, 10.14. Found: C, 62.19; H, 9.86.

Reaction of 2,2,6,6-tetramethylcyclohexanethione (**6g**) *in THF; formation of* **17**. A solution of **1** (178 mg, 1 mmol) and **6g** (170 mg, 1 mmol) in dry THF (stored for a longer time over sodium, 1 mL) was heated under reflux for 0.5 h. After evaporation of the solvent, the crude mixture was crystallized from hexane to give *diethyl (6,6,10,10-tetramethyl-4-thia-1,2-diazaspiro[4.5]dec-2-ene)-3-phosphonate* (**17**). Yield: 120 mg (35%). Colorless crystals; mp 105–120 °C (decomp.). IR (KBr): 3250*s*, 2982*m*, 2959*m*, 2933*m*, 2868*m*, 1526*m*, 1440*m*, 1246*s* (P=O), 1038*s* (P–O–C), 984*m*, 961*m*, 766*m*, 522*m*. ^{1}H-NMR ($CDCl_3$): 1.01 (*s*, 2 Me), 1.09 (*s*, 2 Me), 1.36 (*t*, $J_{H,H} = 7.0$ Hz, 2 *Me*CH_2O), 1.40–1.65 (*m*, 3 CH_2), 4.10–4.24 (*m*, 2 MeC*H*$_2$O), 6.65 (br *s*, NH). ^{13}C-NMR ($CDCl_3$): 16.3 (*d*, $^{3}J_{C,P} = 6.4$ Hz, 2 *Me*CH_2O), 18.1 (CH_2), 25.2 (2 Me), 29.4 (2 Me), 36.5 (2 CH_2), 41.8 (2 C_q), 63.1 (*d*, $^{2}J_{C,P} = 5.2$ Hz, 2 Me*C*H_2O), 100.7 (C_q), 131.6 (*d*, $^{1}J_{C,P} = 242$ Hz, C_q). ^{31}P-NMR ($CDCl_3$): 6.6. CI-MS (NH_3): 350 (18), 349 (100, $[M+1]^+$), 321 (5), 264 (7), 223 (6). Anal. Calcd for $C_{15}H_{29}N_2O_3PS$: C, 51.71; H, 8.39; N, 8.04. Found: C, 51.82; H, 7.90; N, 7.81.

Reaction of thiocamphor (**6h**) *with* **1**. A solution of **6h** (168 mg, 1 mmol) and **1** (178 mg, 1 mmol) in dry THF (1 mL) was heated under reflux for 6 h. After evaporation of the solvent, the crude mixture was separated chromatographically on a SiO_2 column (CH_2Cl_2/Et_2O 1:1) to give *diethyl [(1,7,7-trimethyl-bicyclo[2.2.1]hept-2-en-2-yl)sulfanyl]methanephosphonate* (**18**). Yield: 200 mg (63%). Yellow, thick oil. IR (neat): 2983*s*, 2954*s*, 2911*s*, 1563*m*, 1474*m*, 1452*m*, 1389*s*, 1375*s*, 1258*s* (P=O), 1054*s* and 1026*s* (P–O–C), 965*s*, 827*m*, 821*m*. ^{1}H-NMR ($CDCl_3$): 0.79, 0.81, 1.01 (3*s*, 3 Me), 1.10–2.45 (*m*, 5 H), 1.32 (*t*, $J_{H,H}$ = 7.1 Hz, 2 *Me*CH_2O), 2.94 (*d*, $^2J_{H,P}$ = 16.0 Hz, CH_2P), 3.95–4.40 (*m*, 2 MeC*H*$_2$O), 5.58 (*d*, $J_{H,H}$ = 4.3 Hz, =CH). ^{13}C-NMR ($CDCl_3$): 125.1 (*s*, C=*C*H), 143.5 (*d*, $^3J_{C,P}$ = 7.5 Hz, *C*=CH). ^{31}P-NMR ($CDCl_3$): 24.09. CI-MS (NH_3): 320 (18), 319 (100, $[M+1]^+$), 287 (30). Anal. Calcd for: $C_{15}H_{27}O_3PS$: C, 56.58; H, 8.55, S, 10.07. Found: C, 56.61; H, 8.56, S, 9.89.

ACKNOWLEDGMENTS

We thank the analytical services of our institutes for analyses and spectra. *G. M.* and *S. L.* thank the Rector of the University of Lodz for financial support (Grants 505/712 and 505/710); *H. H.* acknowledges financial support by *F. Hoffmann-La Roche AG*, Basel.

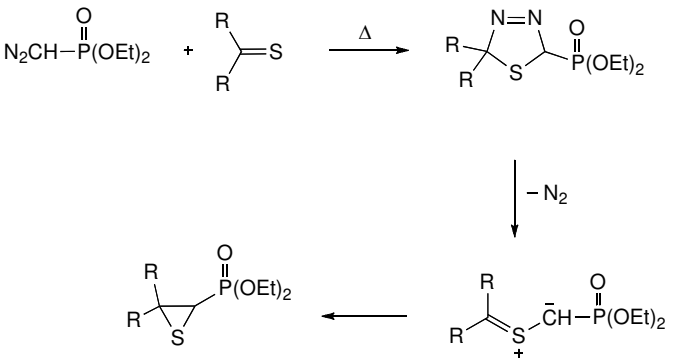
REFERENCES AND NOTES

1. S. Lesniak, G. Mloston, K. Urbaniak, P. Wasiak, A. Linden, and H. Heimgartner, *Tetrahedron*, 2006, **62**, 7776.
2. G. Mloston and H. Heimgartner, *Pol. J. Chem.*, 2000, **74**, 1503.
3. G. Mloston and H. Heimgartner, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products,* ed. by A. Padwa and W. H. Pearson, J. Wiley & Sons, New York, 2002, p. 315.
4. G. Mloston and H. Heimgartner, in *Targets in Heterocyclic Systems - Chemistry and Properties*, ed. by O. A. Attanasi and D. Spinelli, Italian Society of Chemistry, Rome, 2005, Vol. 9, p. 141.
5. A. W. Fokin and A. F. Kolomijec, *Khimija Thiiranov*, Nauka, Moskva, 1978; *Chem. Abstr.*, 1979, **91**, 140705n; W. Ando, N. Choi, and N. Tokitoh, in *Comprehensive Heterocyclic Chemistry II,* ed. by A. R. Katritzky, C. W. Rees, and E. F. Scriven, Vol. 1A, ed. by A. Padwa, Pergamon, Oxford, 1996, p. 173.
6. T. Schirmeister and A. Klockow, *Mini Rev. Med. Chem.*, 2003, **3**, 585.
7. *Handbook in Organophosphorus Chemistry*, ed. by R. Engel, Marcel Dekker, Inc., New York 1992; *A Guide to Organophosphorus Chemistry*, ed. by L. D. Quin, J. Wiley & Sons, New York 2000.

8. M. Kägi, G. Mloston, and H. Heimgartner, *Pol. J. Chem.* 1998, **72**, 678.
9. H. Heimgartner and G. Mloston, in *Electronic Encyclopedia of Reagents in Organic Synthesis*, ed. by L. Paquette, J. Rigby, D. Crich, and P. Wipf, John Wiley & Sons, Chichester, West Sussex, PO 19 88Q, UK, Article RN00430.
10. H. Heimgartner and G. Mloston, in *Electronic Encyclopedia of Reagents in Organic Synthesis*, ed. by L. Paquette, J. Rigby, D. Crich, and P. Wipf, John Wiley & Sons, Chichester, West Sussex, PO 19 88Q, UK, Article RN00431.
11. G. Mloston, A. Majchrzak, M. Rutkowska, M. Woznicka, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2005, **88**, 2624.
12. M. Woznicka, M. Rutkowska, G. Mloston, A. Majchrzak, and H. Heimgartner, *Pol. J. Chem.*, 2006, **80**, 1683.
13. The 4 Me groups of the minor isomer *cis*-**9** appear as two singlets at 1.14 and 1.21 ppm in the ^{1}H-NMR spectrum of the crude mixture of the isomers.
14. The reaction of diazomethane with **6f** leads to a mixture of *exo*- and *endo*-configured spirothiiranes.[15]
15. R. Huisgen, G. Mloston, and A. Pröbstl, *Heteroatom Chem.*, 2001, **12**, 136.
16. There is no proof of the configurations of the products. Therefore, a mixture of two diastereomers of *endo*-**12** is possible as well as a mixture of an *endo* and an *exo* isomer.[14]
17. G. Mloston and R. Huisgen, *Tetrahedron Lett.*, 1985, **26**, 1053.
18. The enhanced thermal stability of **14** may be the reason for the observed isomerization instead of N_2 elimination. The steric hindrance in 2,2,6,6-tetramethylcyclohexane derivatives of type **14** obtained from the reaction of **6g** with diazomethane leads to slower elimination of N_2 in comparison with other spirocyclic 2,5-dihydro-1,3,4-thiadiazoles.[19]
19. R. Huisgen, H. Giera, and K. Polborn, *Tetrahedron*, 2005, **61**, 6143.
20. G. Mloston and R. Huisgen, *Tetrahedron Lett.*, 1989, **30**, 7045.
21. D. Seyferth, R. S. Marmor, and P. Hilbert, *J. Org. Chem.*, 1971, **36**, 1379.
22. E. W. Elam and H. E. Davis, *J. Org. Chem.*, 1967, **32**, 1563.
23. J. W. Greidanus, *Can. J. Chem.*, 1970, **48**, 3530.
24. P. Klages and J. Voß, *Chem. Ber.*, 1980, **113**, 2255.
25. R. Huisgen, L. Fisera, H. Giera, and R. Sustmann, *J. Am. Chem. Soc.*, 1995, **117**, 9671.
26. D. H. R. Barton, F. S. Guziec, and I. Shahak, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1794.

Graphical Abstract

FORMATION OF PHOSPHONYLATED THIIRANES IN THE REACTION OF A DIAZOMETHANEPHOSPHONATE AND CYCLOALIPHATIC THIOKETONES



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1,3-Dipolar cycloaddition Phosphonates Thiiranes Thiocarbonyl ylides Thioketones